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EXAMINER	
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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/972,758	Applicant(s) Montano et al
	Examiner Ungar	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *THREE* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 14, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) *7-26* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *7,8*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Election filed April 14, 2003 (Paper No. 11) in response to the Office Action of December 31, 2002 (Paper No. 9) is acknowledged and has been entered. Claims 1-26 are pending in the application and Claims 7-24 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-6 and 25-26 are currently under prosecution.

2. Applicant's election without traverse of Group I, claims 1-6 and 25-26 in Paper No. 11 is acknowledged.

Specification

3. The disclosure is objected to because of the following informalities:

The specification on page 1 should be amended to reflect the status of the parent application serial number 60/238,187. Further, Applicant cannot claim priority to the provisional patent application, rather, the Applicant can claim benefit of the provisional patent application, for example,

"This application claims benefit to provisional application **********, filed **, now abandoned."

Appropriate correction is required.

Claim Objections

4. Claims 25-26 are objected to because claim 25 recites a sequence which is complementary to a second contiguous sequence in SEQ ID NO:2. It appears that this is an inadvertent typographical error as SEQ ID NO:2 is an amino acid sequence. The objection can be obviated by amending claim 25 to delete reference to SEQ ID NO:2 and to substitute reference thereto to SEQ ID NO:1.

Claim Rejections - 35 USC § 112

5. Claims 1-6 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising SEQ ID NO:1 or an isolated polynucleotide encoding SEQ ID NO:2 and the complete complement thereof or a polynucleotide which hybridizes to SEQ ID NO:1 under highly stringent conditions, does not reasonably provide enablement for an isolated polynucleotide comprising 200 nucleotides of SEQ ID NO:1 or the complement thereof, a nucleic acid sequence of at least 200 nucleotides which hybridizes under stringent conditions to SEQ ID NO:2 or hybridizes under stringent conditions/highly stringent conditions to the complement thereof, an isolated polynucleotide that encodes a functional equivalent of SEQ ID NO:2 which comprises a sequence which is at least 85% identical to SEQ ID NO:2, a primer set for amplifying an EDG1 transcript. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The claims are drawn to an isolated polynucleotide comprising 200 nucleotides of SEQ ID NO:1 or the complement thereof, a nucleic acid sequence of at least 200 nucleotides which hybridizes under stringent conditions to SEQ ID NO:2 or hybridizes under stringent conditions/highly stringent conditions to the complement thereof, an isolated polynucleotide that encodes a functional equivalent of SEQ ID NO:2 which comprises a sequence which is at least 85% identical to SEQ ID NO:2, a primer set for amplifying an EDG1 transcript.. This includes a whole universe of variant polynucleotides which encode a whole universe of variant polypeptides. The specification teaches that EDG1 protein, SEQ ID NO:1 is a

tumor suppressor which is useful for differentiating normal breast tissue cells from cancerous breast tissue cells (see abstract) and that functional equivalents of EDG1 are those that have equivalent function, i.e. they are immunologically cross reactive or biologically active equivalents (p. 12, lines 27-30). It is noted that no definition has been provided or a biologically active equivalent. The functional equivalents have an altered sequence wherein one or more of the amino acids in the functional equivalents is substituted, deleted or added to (para bridging pages 12-13). SEQ ID NO: 1 encodes SEQ ID NO:2. The present invention also encompasses isolated polynucleotides whose sequence is the complement of SEQ ID NO:1, polynucleotides that hybridize under stringent conditions to SEQ ID NO:1 or the complement thereof (p. 16, lines 26-31) as well as polynucleotides encoding variants of SEQ ID NO:2 wherein the variants have at least 85% identity to SEQ ID NO:2 (p. 17, lines 15-22). The specification teaches that the term complementary refers to the natural binding of the polynucleotides under permissive salt and temperature conditions by base pairing (p. 18, lines 1-6). The invention also encompasses isolated polynucleotides which are alleles of the genes which encode the EDG1 protein. An allele is an alternative form of the gene which may result from one or more mutations (p. 19, lines 10-18). The invention also encompasses altered polynucleotides which encode the EDG1 protein or functional equivalents thereof. EDG1 polynucleotides are useful for detecting, defining borders or grading mammary epithelial cell carcinomas (p. 22, lines 17-27). The EDG1 polynucleotides and proteins encoded thereby may be used to block the growth or decrease the proliferation of hormone responsive cancer cells (p. 25, lines 12-20).

The polynucleotides encoding the EDG1 protein or a functional equivalent thereof are useful for gene therapy (para bridging pages 25-26). The encoded protein or functional equivalent thereof can be used to inhibit proliferation of cancer cells (p. 28, lines 7-17.

One cannot extrapolate the teaching of the specification to the scope of the claims because protein chemistry is probably one of the most unpredictable areas of biotechnology. In particular, Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological

activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, with differences in the encoded polypeptide of up to 14.99% and differences drawn complements, differences drawn to isolated polynucleotides comprising at least 200 nucleotides of SEQ ID NO:1, wherein the complement thereof is not even required to be complementary to SEQ ID NO:1 and the difference between these species and the 1070 residue SEQ ID NO:1 is greater than 80%, given the teachings above, the effects of these differences upon the encoded polypeptide could not be predicted based on sequence similarity with SEQ ID NO:2 nor would it be expected to be the same as that of SEQ ID NO:2. In addition, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison

analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2). Clearly, given not only the teachings of Bowie et al, Lazar et al and Burgess et al but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, with the identified dissimilarities of the claimed polynucleotides encoding polypeptides, it could not be predicted, based on sequence similarity with SEQ ID NO:2, nor would it be expected that the function of the encoded proteins would be the same as that of SEQ ID NO:2. Further, given the breadth of the claims, if the

claimed polynucleotides do not encode SEQ ID NO:2, one would not know how to use them for the reasons set forth above. In particular, as drawn to the complements thereof and the hybridizing polynucleotides, when given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species and it would be expected that a substantial number of the complementary/hybridizing polynucleotides encompassed by the claims **would not** share either structural or functional properties of SEQ ID NO:1 or encode proteins that share either structural or functional properties with SEQ ID NO:2. The specification fails to provide an enabling disclosure for how one would use such polynucleotides. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art on how to use the broadly claimed species. For the above reasons, undue experimentation would be required to practice the claimed invention. The rejection can be obviated by amending the claims to recite:

for example, claim 1a, an isolated polynucleotide consisting of 200 nucleotides of SEQ ID NO:1 or the complete complement thereof

for example, claim 1b a nucleic acid which completely hybridizes to a nucleic acid sequence consisting of 200 nucleotides, which completely hybridizes to Seq ID NO:1 or the complete complement thereof under highly stringent conditions

for example, claim 3, an isolated polynucleotide comprising a sequence which encodes SEQ ID NO 2:

for example claim 25, a primer set for amplifying SEQ ID NO:1 comprising a primer set comprising a sequence which is identical to a first contiguous sequence in

SEQ ID NO:1 and a second primer comprising a sequence which is completely complementary to a second contiguous a second contiguous sequence in SEQ ID NO:1, wherein the second contiguous sequence is downstream of said first contiguous sequence.

6. Claims 1-3, 6, 25, 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1 which encodes SEQ ID NO:2 and therefore the written description is not commensurate in scope with the claims drawn to an isolated polynucleotide comprising 200 nucleotides of SEQ ID NO:1 or the complement thereof, a nucleic acid sequence of at least 200 nucleotides which hybridizes under stringent conditions to SEQ ID NO:2 or hybridizes under stringent conditions/highly stringent conditions to the complement thereof, an isolated polynucleotide that encodes a functional equivalent of SEQ ID NO:2 which comprises a sequence which is at least 85% identical to SEQ ID NO:2, a primer set for amplifying an EDG1 transcript.

The claims are drawn to an isolated polynucleotide comprising 200 nucleotides of SEQ ID NO:1 or the complement thereof, a nucleic acid sequence of at least 200 nucleotides which hybridizes under stringent conditions to SEQ ID NO:2 or hybridizes under stringent conditions/highly stringent conditions to the complement thereof, an isolated polynucleotide that encodes a functional equivalent

of SEQ ID NO:2 which comprises a sequence which is at least 85% identical to SEQ ID NO:2, a primer set for amplifying an EDG1 transcript.

The specification discloses an isolated cDNA sequence, SEQ ID NO: 1, which encodes, SEQ ID NO. 2. The claims, as written, however, encompass polynucleotides which vary substantially in length and also in nucleotide composition. In particular the specification teaches that EDG1 protein functional equivalents may vary structurally from SEQ ID NO:2, wherein one or more of the amino acids is substituted, deleted, or added to (pages 12-13). It is noted that the specification does not define the phrase biologically active equivalent in a limiting fashion thus the claim clearly reads, for example, on the ability of the equivalent to be proteolytically cleaved or to be bound by an antibody, any antibody, which reads on a whole universe of polynucleotides which encode a polypeptide whose structure and function are not those of SEQ ID NO:2.

Further, as drawn to the complements and the species hybridizing under "stringent" conditions, it is art recognized that complements may be complete or partial complements. For example, as taught by US Patent No. 5,912,143 the term complementary refers to the natural binding of polynucleotides under permissive salt and temperature conditions and specifically teaches that complementarity between two single-stranded molecules may be "partial" or it may be "complete" (col 5, lines 19-32). It is clear that the "stringent" conditions defined in the specification would allow the hybridization of a substantial number of related polynucleotides whose structure and function would not be those of SEQ ID NO:1. When given the broadest reasonable interpretation, the claims are clearly intended to encompass a

variety of species. Clearly, it would be expected that a substantial number of the complementary polynucleotides encompassed by the claims **would not** share either structural or functional properties with polynucleotides that encode SEQ ID NO:1 or encode proteins that share either structural or functional properties with SEQ ID NO:2.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The specification proposes to discover other members of the genus by using standard screening assays There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides

encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

In particular as drawn to a primer set for amplifying an EDG1 transcript, it is noted that the specification teaches that polynucleotides (clearly drawn to EDG1 transcripts) which encode an EDG1 protein, particularly alleles of the genes which encode an EDGE1 protein, may be screened using a probe to screen a genomic library or cDNA library or with antibodies immunospecific for an EDG1 protein (p. 20, lines 1-10), thus the claims read on primers that will amplify a genomic variant of SEQ ID NO:1 wherein the only structural equivalent required is a SEQ ID NO:2 epitope. The specification fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Harris et al. J. of The Am Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising SEQ ID NO: 1 or fragments thereof.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient

to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Therefore only an isolated DNA molecule comprising a DNA sequence consisting of SEQ ID NO:1 or a polynucleotide encoding SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 1, 2, 25 are rejected under 35 USC 102(b) as being anticipated by Boehringer Mannheim Biochemicals, 1994 Catalog, p. 93).

The claims are drawn to an isolated polynucleotide comprising a sequence selected from the group of a nucleotide of a least 200 nucleotides which is a portion of SEQ ID NO:1 or a complement thereof and a nucleic acid of at least 200

nucleotides which hybridizes to SEQ ID NO:1 or a complement thereof under stringent conditions.

It is noted that the term "complement" is undefined by the specification, thus the term "complement" is interpreted to include both a complete complement and a partial complement thereof since the art recognizes that the complement encompasses this range of complementarity.

The Boehringer Mannheim teaches a kit comprising random primers that encompass all possible 6-nucleotide sequences (see page 93, Catalog No. 1034 731/1006 924), and therefore a subset of the random primers would include the complement of the claimed polynucleotides and would hybridize under stringent, highly stringent conditions to the claimed complement. Further, a subset of the primers would include those that are identical to a first contiguous sequence in SEQ ID NO:1 and a second subset of the random primers would include a second primer comprising a sequence which is complementary to a second contiguous sequence in downstream of the first contiguous sequence. All of the limitations of the claims are met.

9. Claims 1 and 2 are rejected under 35 USC 102(e) as being anticipated by US20030073623.

The claims are drawn to an isolated polynucleotide comprising a sequence selected from the group consisting of a nucleotide of a least 200 nucleotides which is a portion of SEQ ID NO:1 or a complement thereof and a nucleic acid of at least 200 nucleotides which hybridizes to SEQ ID NO:1 or a complement thereof under stringent conditions, highly stringent conditions.

US20030073623 teaches an isolated polynucleotide comprising a sequence of 371 contiguous nucleic acid residues that are identical to the complete complement of residues 709-1080 of SEQ ID NO:1, see Sequence search us-09-972-758a-1.rnpb, result 4 . Given the complete complement of residues 709-1080, one would immediately envision residues 709-1080 of SEQ ID NO:1 and the prior art polynucleotide or complete complement thereof will hybridize to SEQ ID NO:1 or the complete complement thereof under stringent conditions, highly stringent conditions. All of the conditions of the claims are met.

10. Claims 1-5 are rejected under 35 USC 102(b) as being anticipated by WO9842739.

The claims are drawn to an isolated polynucleotide comprising a sequence selected from the group of a nucleotide of a least 200 nucleotides which is a portion of SEQ ID NO:1 or a complement thereof and a nucleic acid of at least 200 nucleotides which hybridizes to SEQ ID NO:1 or a complement thereof under stringent conditions, highly stringent conditions, a polynucleotide encoding SEQ ID NO:2, a functional equivalent at least 85% identical to SEQ ID NO:2, which will cross reactive with an antibody raised using SEQ ID NO:2 which would inhibit proliferation of MCF-7 cells.

WO9842739 teaches a polynucleotide with 99.8 local similarity to 99.7% of SEQ ID NO:1, see Sequence search us-09-972-758a-1.rnp result 2. Given the identity, one would immediately envision the complete complement thereof .The sequence will hybridize to the complete complement of SEQ ID NO:1 under stringent conditions, highly stringent conditions which encodes a polypeptide with

100% identity to SEQ ID NO:2, see Sequence search us-09-972-758a-2.rag, result 1 which is clearly the functional equivalent of SEQ ID NO:2 wherein an antibody raised to SEQ ID NO:2 will bind, which would inhibit proliferation of MCF-7 cells, given that the sequence of the encoded polypeptides is identical. All of the limitations of the claims are met.

11. Claims 3-5, 25 are rejected under 35 USC 102(b) as being anticipated by Kusuhara et al (Biomed. Res., 1999, 20:273-279).

The claims are drawn to an isolated polynucleotide encoding SEQ ID NO:2, a functional equivalent at least 85% identical to SEQ ID NO:2, wherein an antibody raised to SEQ ID NO:2 will bind, which would inhibit proliferation of MCF-7, and a primer set for amplifying the transcript.

Kusuhara et al teach a polynucleotide that encodes a polypeptide with 100% identity to SEQ ID NO:2, see Sequence search us-09-972-758a-1.rge, result 2. which is clearly the functional equivalent of SEQ ID wherein an antibody raised to SEQ ID NO:2 will bind, which would inhibit proliferation of MCF-7 cells, given that the sequence of the encoded polypeptide is identical. Kusuhara et al further teach primers for amplifying the transcript (see p. 274, col 2, Molecular Cloning). All of the limitations of the claims are met.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

13. Claim 6 is rejected under 35 USC 103 as being unpatentable over WO9842739, *Supra* or Kusuhara et al, *Supra* in view of US Patent No. 4,889,806 and Sambrook et al (Molecular Cloning, a Laboratory Manual, 1989, Cold Spring Harbor Press, p. 16.3-4.

The claims are drawn to an isolated polynucleotide which encodes EDG1 protein or a functional equivalent thereof wherein said polynucleotide comprises part of an expression vector.

US Patent No. 4,889,806 teaches vectors, or plasmids defined as Yeast Artificial Chromosome (YAC) vectors (col 3, lines 42-44) and teach that with the

advent of recombinant DNA and molecular cloning technology it is now conventional to transfer genetic information into any source, using small plasmids constructed *in vitro*, and then transferred into host cells and clonally propagated and that most DNA cloning systems have a capacity for only small segments of exogenous DNA and are well suited to the analysis and manipulation of typical genes and that the YAC cloning system allows the cloning of large segments of exogenous DNA (col 1, lines 18-50) and have significant utility in the analysis of megabase-pair regions of DNA which lead to mapping of large regions of DNA and the cloning of candidate genes involved in disease.

Sambrook et al teach that cloned genes are conventionally expressed using expression vectors and that expression of cloned proteins have been used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; (4)to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins (para bridging pages 16.3 and 16.4)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine a cDNA, containing the isolated polynucleotide of WO9842739, *Supra* or Kusuhara et al with the methods of US Patent No. 4,889,806 to produce vectors for the expression of the nucleotides because Sambrook et al and US Parent No. 4,889,806 teach that cDNA is

conventionally expressed using a vector system. One of ordinary skill in the art would have been motivated to combine the cDNA of WO9842739, *Supra* or Kusuhara et al and the methods of US Patent No. 4,889,806 because WO9842739 specifically teaches that the encoded protein is predicted to have biological activities which make them suitable for treating, preventing or ameliorating medical condition in humans and animals and because Sambrook et al teach that expression of cloned proteins have been used to (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; (4) to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins which would be useful in characterizing the involvement of the gene in the etiology of the disease and one would be motivated to use the YAC cloning system because US Patent No. 4,889,806 specifically teaches that the system has significant utility in the analysis of megabase-pair regions of DNA which would lead to the cloning of candidate genes involved in disease.

14. Claims 25 and 26 are rejected under 35 USC 103 as being unpatentable over Kusuhara et al, *Supra* in view of US Patent No. 4,683,202.

The claims are drawn to a primer set for amplifying an ADG1 transcript, comprising a first primer comprising a sequence which is identical to a first contiguous sequence in SEQ ID NO:1 and a second primer comprising a sequence

which is complementary to a second contiguous sequence in SEQ ID NO:1, wherein the primers are each at least 12 nucleotides in length.

Kusuhara et al teach as set forth above and further teach the PCR amplification of a polynucleotide that encodes a polypeptide with 100% identity to SEQ ID NO:2 wherein the amplification was done by PCR with primers wherein the primers were an anchor primer and a gene specific primer for the cDNA fragment, wherein the amplified fragments were used for sequencing as well as to screen a human placenta cDNA library for positive clones (p. 274, col 2, molecular cloning).

US Patent No. 4,683,202 teaches a method of amplifying any desired specific nucleic acid sequence contained in a nucleic acid or mixture thereof (see abstract) wherein two primers are used, the first primer comprising a sequence which is identical to a first contiguous sequence in one strand and a second primer comprising a sequence which is complementary to a second contiguous sequence are selected (col 2, lines 60-69), the primers must be sufficiently long to prime the synthesis of extension products in the presence of an inducing agent, typically, primers contain 15-25 or more nucleotides (col 4, lines 24-50).

It would have been prima facie obvious to one of ordinary skill in the art, and one would have been motivated to use substitute two primers, the first primer comprising a sequence which is identical to a first contiguous sequence in one strand of the polynucleotide of Kusuhara et al and a second primer comprising a sequence which is complementary to a second downstream contiguous sequence of Kusuhara et al wherein the primers are 15-25 nucleotides because US Patent No. 4,683,202, which is the original patent for the PCR amplification process,

specifically teaches that these kinds of primers are useful for amplifying any desired specific nucleic acid. One of ordinary skill in the art would have expected to be able to amplify the polynucleotide of Kusuhara et al with a reasonable expectation of success.

15. No claims allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Susan Ungar
Primary Patent Examiner
June 22, 2003